



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/812,393	03/05/1997	LINDA A. SHERMAN	313332000100	2284

7590 12/31/2001

Robert L. Buchanan
EDWARDS & ANGELL LLP
PO Box 9169
Boston, MA 02209

EXAMINER

WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
----------	--------------

1633

DATE MAILED: 12/31/2001

35

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/812,393

Applicant(s)

SHERMAN ET AL.

Examiner

Michael Wilson

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 6-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1633

DETAILED ACTION

The amendment filed 11-30-00, paper number 25, has been entered. The arguments therein have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

This application contains claims 6-21 drawn to an invention nonelected with traverse in Paper No. 20. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Specification

The specification is objected to because page 13, line 9, has two blanks. Blanks are improper and should be filled in with the appropriate information. Applicants are reminded that addition of such information to the specification may result in a new matter rejection. Support for amendments should be pointed to by page and line number.

Claim Objections

A comma should be placed in claim 1 after "Bage".

Art Unit: 1633

Claim Rejections - 35 USC § 112

1. Claims 1-5 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolating a nucleic acid molecule encoding a TAA-specific mouse TCR comprising: 1) administering a TAA to a transgenic mouse whose genome comprises a nucleic acid sequence encoding HLA-A2 operably linked to a promoter, wherein said mouse functionally expresses HLA-A2 on the surface of an APC and presents the TAA on the surface of the APC in the context of HLA-A2 and wherein the TAA is selected from the group consisting of Her-2/neu, RAS, tyrosinase, MART, Gp100, Mage, Bage, and MUC-1, 2) isolating TAA-specific CTL from the mouse, and 3) isolating a nucleic acid molecule encoding TAA-specific mouse TCR from the TAA-specific CTL, does not reasonably provide enablement for using the method with p53. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 remains rejected for reasons of record regarding p53. Applicants state this rejection has been address by the response, but it is not clear that p53 has been deleted from the claim as it remains in the "clean" copy of the claim in brackets.

2. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1633

Claim 1 as newly amended is indefinite because it is unclear if "[p53]" is part of the claim.

Claim 1 is indefinite because the phrases "encoding at least one of the variable regions of each of the α and β chains" and "one of each of the variable regions" as newly amended are indefinite. It remains unclear whether applicants intend to claim at least one variable region which can be either α or β chain or whether applicants intend to claim at least one α chain and one β chain.

Claims 4 is indefinite because the "cloning or amplifying step" in claim 1 does not "comprise" anything, so it cannot "further comprise" anything.

Claim Rejections - 35 USC § 103

3. Claims 1-5 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Man (1994, J. Immunol., Vol. 153, pages 4458-4467) in view of Cole (April 1995, FASEB Journal, Vol, 9, page A801, abstract 4638) for reasons of record.

Man taught immunizing transgenic mice expressing HLA-A2.1 with M1₍₅₈₋₆₆₎, isolating CTL from the mice that lyse the M1, amplifying DNA encoding the α and β chain of the M1-specific TCR by PCR (page 4459, column 1, "influenza-specific CTL from HLA-A2.1 transgenic mice"; page 4459, column 2, "PCR amplification and sequencing of TCR α - and β -chain cDNA). The primers used by Man were mouse α and β TCR-specific primers V β 8, V β 5 and V β 6 which are the primers V β 8.1, V β 8.2, V β 8.3, V β 5.1 and V β 6 primers in Fig. 6. Man did not

Art Unit: 1633

teach using the transgenic mouse to isolate TAA-specific TCR. However, Cole taught generating MART-1-specific, HLA-A2 restricted CTL and isolating the TCR gene from the CTL (see entire abstract). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of isolating TCR genes from transgenic mice taught by Man to obtain TCR genes specific for the MART-1 antigen. One of ordinary skill would have been motivated to replace the M1 antigen with the MART-1 antigen to obtain MART-1 specific TCR *in vivo*.

Applicants argue that Man dissuaded one of ordinary skill from attempting the experiment by stating the transgenic mice are inefficient and the HLA-A2 molecule does not interact well with endogenous CD8 cells in the mouse. Applicants argument is not persuasive because Man obtained mouse TCR recognizing antigen. One of ordinary skill would have been motivated to replace the M1 antigen with the MART-1 antigen to obtain MART-1 specific TCR *in vivo*. Inefficiency would not have been adequate to dissuade the ordinary artisan at the time of filing from repeating the experiment because the method resulted in obtaining a CTL response against the antigen and isolating a mouse TCR recognizing antigen. Applicants have done nothing greater than Man to improve the transgenic mouse or isolate mouse TCR.

Applicants argue Cole does not suggest isolating CTL obtained *in vivo*, particularly from a transgenic mouse expressing HLA-A2. Applicants argument is not persuasive because Cole need not teach all the limitations of the claims. Cole is relied upon because it also taught generating antigen-specific, HLA-A2 restricted CTL and isolating the TCR gene from the CTL.

Art Unit: 1633

One of ordinary skill in the art at the time the invention was made would have every reason to believe the transgenic mice expressing HLA-A2 could also be used to obtain TAA-specific CTL and would have been motivated to use the method of Man to obtain MART-1 specific TCR *in vivo*.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Art Unit: 1633

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-2982.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.
Michael C. Wilson



MICHAEL C. WILSON
PATENT EXAMINER